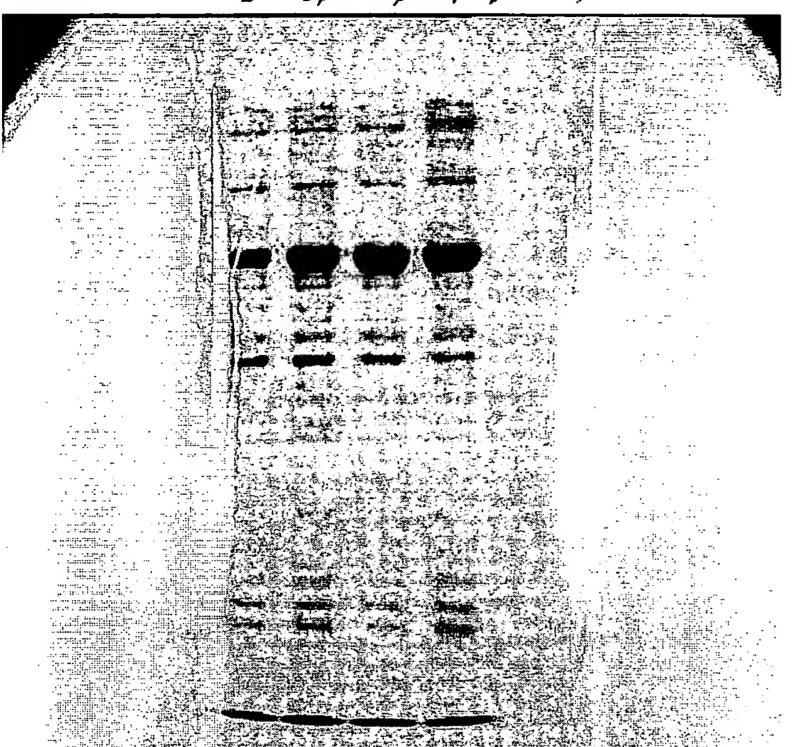
Title: CLONING, OVEREXPRESSIQ THERAPEUTIC USE OF BIOAC'S HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al.

DOCKET NO.: 078728/0106

Figure 5: SDS-PAGE showing expression of HAL in E. coli?

Lanes:

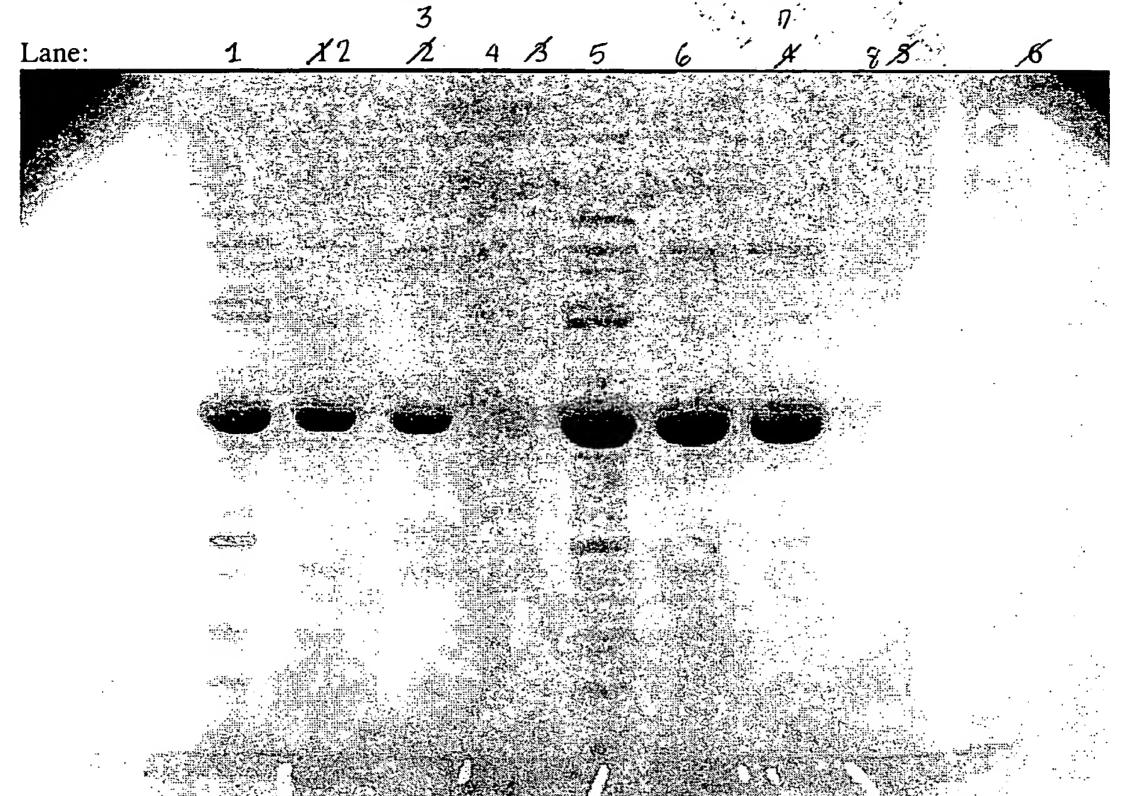




Title: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOA HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al.

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Figure 6: SDS-PAGE showing purification of HAL from E. coli





### Title: CLONING, OVEREXPRESSIC AND THERAPEUTIC USE OF BIOACE HISTIDINE AMMONIA LYASE

Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106

### Figure 13: Histidine ammonia lyase peptide sequence pileup

_		
HUTH_RHIME		
-		A Fac
HUTH_MOUSE		
MPRYTVHVRGEWLAVE	CQDGKLTVGWLGREAVRRYMKNKPDNGGFTSVDEVQFLVHRCKG	
HUTH RAT		
MPRYTVHVRGEWLAVE	CQDGKLSVGWLGREAVRRYMKNKPDNGGFTSVDEVRFLVRRCKG	
HUTH HUMAN		
<del>_</del>	CQDAQLTVGWLGREAVRRYIKNKPDNGGFTSVDDAHFLVRRCKG	
HUTH CAEEL	-MRLQVQIGTECVVVPCKP-DDTIHAVAKKSVEKLRRLRPK	
LPLADDYFEVRRTVG	-MKDQVQIGIECVVVFCKF-DDIIMAVAKKSVEKLKPK	-
		•
HUTH_BACS		
HUTH_STRGR		
_		
HUTH_CORY		
_		
HUTH PSEPU		
_		
HUTH RHIME		
-		
HUTH MOUSE	LGLLDNEDELEVALEDNEFVEVVIEGDVMSPDFIPSQ	ADECUET VCEVO
	EGEDDUEDEE VALEDUE VEVVIEGDVMSPDF 1 PSQ	PEGVELISKIK
		`
HUTH_RAT	LGLLDNEDLLEVALEDNEFVEVVIEGDVMSPDFIPSQ	PEGVFLYSKYR
<del>-</del>		
HUTH_HUMAN	LGLLDNEDRLEVALENNEFVEVVIEGDAMSPDFIPSQ	QPEGVYLYSKYR
_		
HUTH_CAEEL		
NSLLDPEDLVSDVLKD	SDFIIVAASVEETEDAKEAKKQEEIDNARAEIEKIDNRRRKVSF	
HUTH BACS		
_		
-		
-		
 HUTH_STRGR -		
 HUTH_STRGR - HUTH_CORY -		
HUTH_STRGR - HUTH_CORY - HUTH_PSEPU	· · · · · · · · · · · · · · · · · · ·	
HUTH_STRGR - HUTH_CORY - HUTH_PSEPU FELTLKPGTLTLAQLF	AIHAAPVRLQLDASAAPAIDASVACVEQIIA	
 HUTH_STRGR - HUTH_CORY - HUTH_PSEPU FELTLKPGTLTLAQLF HUTH_RHIME	AIHAAPVRLQLDASAAPAIDASVACVEQIIA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU FELTLKPGTLTLAQLE HUTH_RHIME MTVILRPGSVPLSDLE	· · · · · · · · · · · · · · · · · · ·	
HUTH_STRGR HUTH_CORY HUTH_PSEPU FELTLKPGTLTLAQLF HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE	AIHAAPVRLQLDASAAPAIDASVACVEQIIA  TIYWTGAPARLDAAFDAGIAKAAARIAEIVA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU FELTLKPGTLTLAQLF HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE	AIHAAPVRLQLDASAAPAIDASVACVEQIIA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE	AIHAAPVRLQLDASAAPAIDASVACVEQIIA  TIYWTGAPARLDAAFDAGIAKAAARIAEIVA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_PSEPU HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA	
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HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_PSEPU HUTH_RHIME HUTH_RHIME HUTH_MOUSE HUTH_MOUSE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL	AIHAAPVRLQLDASAAPAIDASVACVEQIIA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_PSEPU HUTH_RHIME HUTH_RHIME HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL ADSLAPMVLAPPTKLI	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK	
HUTH_STRGR HUTH_CORY HUTH_PSEPU FELTLKPGTLTLAQLF HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL ADSLAPMVLAPPTKLI HUTH_BACS	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK LUUNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK	
HUTH_STRGR HUTH_CORY HUTH_PSEPU FELTLKPGTLTLAQLE HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL ADSLAPMVLAPPTKLI HUTH_BACS MVTLDGSSLTTADVAF	AIHAAPVRLQLDASAAPAIDASVACVEQIIA	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_RHIME HUTH_RHIME HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL ADSLAPMVLAPPTKLI HUTH_BACS MVTLDGSSLTTADVAF HUTH_STRGR	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK LUUNLGKGRYKIKLTPTAEKRVQKSREVIDSIIK LUGNSLLPEDLVRCEKGECAIQLSMESEDRIRKARTFLEKIAS VLFDFEEAAASEESMERVKKSRAAVERIVR	
HUTH_STRGR HUTH_CORY HUTH_PSEPU FELTLKPGTLTLAQLE HUTH_RHIME MTVILRPGSVPLSDLE HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL ADSLAPMVLAPPTKLI HUTH_BACS MVTLDGSSLTTADVAF HUTH_STRGR MDMHTVVVGTSGTTAE	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK LUUNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK	
HUTH_STRGR HUTH_CORY HUTH_PSEPU HUTH_RHIME HUTH_RHIME HUTH_MOUSE HUTH_MOUSE EPEKYIALDGDSLSTE HUTH_RAT EPEKYIALDGDSLSTE HUTH_HUMAN EPEKYIELDGDRLTTE HUTH_CAEEL ADSLAPMVLAPPTKLI HUTH_BACS MVTLDGSSLTTADVAF HUTH_STRGR MDMHTVVVGTSGTTAE HUTH_CORY	AIHAAPVRLQLDASAAPAIDASVACVEQIIA TIYWTGAPARLDAAFDAGIAKAAARIAEIVA DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK DLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK LUUNLGKGRYKIKLTPTAEKRVQKSREVIDSIIK LUGNSLLPEDLVRCEKGECAIQLSMESEDRIRKARTFLEKIAS VLFDFEEAAASEESMERVKKSRAAVERIVR	



### Title: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al.

nventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106 44.

### Figure 13 contid.

HUTH PSEPU

EDRTAYGINTGFGLLASTRIASHDLENLQRSLVLSHAAGIGAPLDDDLVRLIMVLKINSL HUTH RHIME

GNAPVYGINTGFGKLASIKIDSSDVATLQRNLILSHCCGVGQPLTEDIVRLIMALKLISL HUTH MOUSE

ERTVVYGITTGFGKFARTVIPANKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL HUTH RAT

ERTVVYGITTGFGKFARTVIPANKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL HUTH HUMAN

EKTVVYGITTGFGKFARTVIPINKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL HUTH CAEEL

EHRAVYGVTTGFGTFSNVTIPPEKLKKLQLNLIRSHATGYGEPLAPNRARMLLALRINIL HUTH BACS

DEKTIYGINTGFGKFSDVLIQKEDSAALQLNLILSHACGVGDPFPECVSRAMLLLRANAL HUTH STRGR

KPEPVYGVSTGFGALASRHIGTELRAQLQRNIVRSHAAGMGPRVEREVVRALMFLRLKTV HUTH CORY

ADTPVYGISTGFGALATRHIAPEDRAKLQRSLIRSHAAGMGEPVEREVVRALMFLRAKTL

#### HUTH PSEPU

SRGFSGIRRKVIDALIALVNAEVYPHIPLKGSVGASGDLAPLATMSLVLLGEGKARYKGQ HUTH RHIME

GRGASGVRLELVRLIEAMLDKGVIPLIPEKGSVGASGDLAPLAHMAAVMMGHGEAFFAGE HUTH MOUSE

AKGYSGISLETLKQVIEAFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS HUTH RAT

AKGYSGISLETLKQVIEVFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS HUTH HUMAN

AKGYSGISLETLKQVIEMFNASCLPYVPEKGTVGASGDLAPLSHLALGLVGEGKMWSPKS HUTH CAEEL

AKGHSGISVENIKKMIAAFNAFCVSYVPQQGTVGCSGDLCPLAHLALGLLGEGKMWSPTT HUTH BACS

LKGFSGVRAELIEQLLAFLNKRVHPVIPQQGSLGASGDLAPLSHLALALIGQGEVFFEGE HUTH STRGR

ASGHTGVRPEVAQTMADVLNAGITPVVHEYGSLGCSGDLAPLSHCALTLMGEGEAEGPDG HUTH CORY ASGRS-

VRPVVLETMVGMLNAGITPVVREYGSLGCSGDLAPLSHCALVLMGEGEATDAHG

#### HUTH PSEPU

WLSATEALAVAGLEPLTLAAKEGLALLNGTQASTAYALRGLFYAEDLYAAAIACGGLSV HUTH RHIME -

RMKGDAALKAAGLSPVTLAAKEGLALINGTQVSTALALAGLFRAHRAGQAALITGALST HUTH MOUSE

GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEALERASAIARQADIVAALTL HUTH RAT

GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALTL HUTH HUMAN

GWADAKYVLEAHGLKPVILKPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALTL HUTH CAEEL

GWQPADVVLKKNNLEPLELGPKEGLALINGTQMVTALGAYTLERAHNIARQADVIAALSL HUTH BACS -

RMPAMTGLKKAGIQPVTLTSKEGLALINGTQAMTAMGVVAYIEAEKLAYQTERIASLTI HUTH STRGR

TVRPAGELLAAHGIAPVELREKEGLALLNGTDGMLGMLVMALADLRNLYTSADITAALSL HUTH CORY

DIRPVPELFAEAGLTPVELAEKEGLALVNGTDGMLGOLIMALADLDELLDIADATAAMSV



### Title: CLONING, OVEREXPRESSION TO THERAPEUTIC USE OF BIOACTION HISTIDINE AMMONIA LYASE

Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106

Figure 13 cont'd.

HUTH PSEPU EAVLGSRSPFDARIHE-ARGQRGQIDTAACFRDLLGDSSEVSLSHKNCD

KVQDPYS

HUTH\_RHIME DAAMGSSAPFHPDIQH-CAAIRARSTRAAALRQLLTG-SPIRQSHIEGDE---

RVQDPYC

HUTH MOUSE EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSLLDS-

DHHPSEIAESHRFCDRVQDAYT

HUTH RAT EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSLLDS-

DHHPSEIAESHRFCDRVQDAYT

HUTH HUMAN EVLKGTTKAFDTDIHA-LRPHRGQIEVAFRFRSLLDS-

DHHPSEIAESHRFCDRVQDAYT

HUTH CAEEL DVLKGTTRAYDPDIHR-IRPHRGQNLSALRLRALLHS-

EANPSQIAESHRNCTKVQDAYT

HUTH BACS EGLQGIIDAFDEDIHL-ARGYQEQIDVAERIRFYLSD-SGLTTSQGE-----

LRVQDAYS

HUTH STRGR EALLGTDKVLAPELHA-IRPHPGQGVSADNMSRVLAG-SGLTGHHQDDAP---

RVQDAYS

HUTH CORY EAQLGTDQVFRAELHEPLRPHPGQGRSAQNMFAFLAD-SPIVASHREGDG---

**RVQDAYS** 

HUTH PSEPU

LRCQPQVMGACLTQLRQAAEVLGIEANAVSDNPLVFAAEGDVISGGNFHAEPVAMAADNL

HUTH RHIME IRCQPQVDGACLDLLRSVAATLTIEANAVTDNPLVLSDN-

SVVSGGNFHAEPVAFAADQI

HUTH MOUSE

LRCCPQVHGVVNDTIAFVKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL

HUTH RAT

LRCCPQVHGVVNDTIAFVKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL

HUTH HUMAN

LRCCPQVHGVVNDTIAFVKNIITTELNSATDNPMVFANRGETVSGGNFHGEYPAKALDYL

HUTH\_CAEEL

LRCVPQVHGVVHDTIEFVREIITTEMNSATDNPLVFADREEIISGGNFHGEYPAKALDFL HUTH BACS

LRCIPQVHGATWQTLGYVKEKLEIEMNAATDNPLIFNDGDKVISGGNFHGQPIAFAMDFL

HUTH STRGR VRCAPQVNGAGRDTLDHAALVAGRELASSVDNPVVLPDG-

RVESNGNFHGAPVAYVLDFL

HUTH\_CORY LRCSPQVTGAARDTIAHARLVATRELAAAIDNPVVLPSG-

EVTSNGNFHGAPVAYVLDFL

HUTH PSEPU ALAIAEIGSLSERRISLMMDKHMS-

OLPPFLVENGGVNSGFMIAQVTAAALASENKALSH

HUTH RHIME

ALAVCEIGAISQRRIALLVDPALSLRLPAFLAKKPGLNSGLMIAEVTSAALMSENKQLSH

HUTH MOUSE AIGVHELAR

AIGVHELAAISERRIERLCNPSLS-

ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH

HUTH RAT AIGVHELAAISERRIERLCNPSLS-

ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH

HUTH HUMAN AIGIHELAAISERRIERLCNPSLS-

ELPAFLVAEGGLNSGFMIAHCTAAALVSENKALCH

HUTH CAEEL AIAVAELAQMSERRLERLVNKELS-

GLPTFLTPDGGLNSGFMTVQLCAASLVSENKVLCH

HUTH BACS KIAISELANIAERRIERLVNPQLN-

DLPPFLSPHPGLQSGAMIMQYAAASLVSENKTLAH

HUTH STRGR

AIVAADLGSICERRTDRLLDKNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEMKRLAV

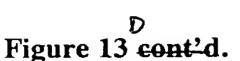
HUTH CORY

AIAVADLGSIAERRTDRMLDPARSRDLPAFLADDPGVDSGMMIAQYTQAGLVAENKRLAV



### Title: CLONING, OVEREXPRESSIONAND THERAPEUTIC USE OF BIOA HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al.

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HUTH PSEPU PHSVDSLPTSANQEDHVSMAPAAGKRLWEMAENTRGVPAIEWLGACQGLDLRKG-LKTS PASVDSTPTSANQEDHVSMACHGARRLLQMTENLFSIIGIEALAAVQGIEFRAP-LTTS HUTH RHIME HUTH MOUSE PSSVDSLSTSAATEDHVSMGGWAARKALRVVEHVEQVLAIELLÁACQGIEFLRP-LKTT PSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRP-LKTT HUTH RAT PSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRP-LKTT HUTH HUMAN HUTH CAEEL PSSVDSIPTSCNQEDHVSMGGFAARKALTVVEHVEAVLAMELLAACQGIEFLKP-LIST PASVDSIPSSANQEDHVSMGTIAARHAYQVIANTRRVTAIEAICALQAVEYRGI-EHAA HUTH BACS HUTH STRGR PASADSIPSSAMQEDHVSMGWSAARKLRTAVDNLARIVAVELYAATRAIELRAAEGLTPA PA-VDSIPSSAMQEDHVSLGWHAARKLPTSVANLRRILAVEMLIAGRALDLRAP-LKPG HUTH CORY AKLEKARQALRSEVA-HYDRDRFFAPDIEKAVELLAKG---S-LTGLLPAGVLPSL---HUTH PSEPU PELQKAAAAVRGVSS-SIEEDRYMADDLKAAGDLVASG---R-LAAAVSAGILPKLEN-HUTH RHIME HUTH MOUSE TPLEKVYDLVRSVVR-PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR TPLEKVYDLVRSVVR-HUTH RAT PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR HUTH HUMAN TPLEKVYDLVRSVVR-

PWIKDRFMAPDIEAAHRLLLEQKVWEVAAPYIEKYRMEHIPESR
HUTH\_CAEEL APLHKIYQLVRSVAPPLNEDRYMKPEIDAVLEMIRENRIWEAVLPHLETLEAMEELDPD

HUTH\_BACS SYTKQLFQEMRKVVP-SIQQDRVFSYDIERLTDWLKK----ESLIPDHQNKELRGMNIHUTH\_STRGR PASEAVVAALRAAGAEGPGPDRFLAPDLAAADTFVREG---R-LVAAVEPVTGPLA--HUTH CORY PATGAVLEVLRSKVA-GPGQDRFLSAELEAAYDLLANG---S-VHKALEAHLPE----

HUTH\_PSEPU
HUTH\_RHIME
HUTH\_MOUSE
PLSPTAFSLESLRKNSATIPESDDL---HUTH\_RAT
HUTH\_HUMAN
PLSPTAFSLQFLHKKSTKIPESEDL---HUTH\_CAEEL
HUTH\_BACS
HUTH\_STRGR

JUN 0 3 2003 G. PADEMARK. CIR.



80

MASAPQITLGLSGATADDVIAVARHEARISISPQVLEELASVRAHIDALASADTPVYGISTGFGALATRHIAPEDRAKLQ

66.18

**%** 

. 48

SWALL: HUTH STRGR

SWALL: CAC2161

983831

SWALL: HUTH DEIRA

SWALL: BAB1615

4

SWALL: Q9KWE4

8

42.0%

46.88

40.48

SWALL: HUTH BACSU

.0%

42

42.28

41.78

SWALL: 09HU85

 $\omega$   $\omega$ 

SWALL: Q9KSQ4

SWALL: Q9KBE6

40.68

200

40

78

41.

SWALL: HUTH PSEPU SWALL: HUTH RHIME

11

10

39.28

SWALL:HUTH\_HUMAN SWALL:HUTH\_CAEEL

13

14

SWALL: Q9HU90

~

38.8% 41.0% 38.68

SWALL: HUTH MOUSE

16

17

SWALL: Q9HLI6

S

38.68

38.2%

SWALL:BAB29407 SWALL:HUTH RAT

18

SWALL: AAG5358

SWALL: Q9HQD5

SWALL: Q9KKE0

19 20

Φ

-MDMHTVVVGTSGTTAEDVVAVARHGARVELSAAAVEALAAARLIVDALAAKPEPVYGVSTGFGALASRHIGTELRAQLQ --MHTVVVGTSGVTASDVLAVARAGARIELSEEAVAALAAARSVVDALAAKPDPVYGVSTGFGALATRHISPELRGRLQ ----MILDRDLNLEQFISVVRHGEQVELSAAARERIARARTVIEQIVEGDTPIYGVNTGFGKFENVQIDRSQLAQLQ ----VPLHHLADIYWNNGSAKLDPSFDAAVLKGAARIAEIAAGNAPVYGINTGFGKLASIKIDAADLATLQ --VPLHHLADIYWNNGSAKLDPSFDAAVLKGAARIAEIAAGNAPVYGINTGFGKLASIKIDAADLATLQ --MVTLDGSSLTTADVARVLFDFEEAAASEESMERVKKSRAAVERIVRDEKTIYGINTGFGKFSDVLIQKEDSAALQ -MLHLMIKPGQLSLKQLRQVSRSPVVLSLDPEAIPAIAESAQVVEQVISEGRTVYGINTGFGLLANTKIAPQDLETLQ --MSLHLKPGQLTLADLRQAYLAPVRLSLDPSADAPIAASVACVENIIAEGRTAYGINTGFGLLASTRISPADLEKLQ -MTNLKLLDGRSLSLHDLHRIIYEGETVGASDESMEKVKQSRKAVEQIVADEKIIYGITTGFGKFSDIFIDPDDVENLQ --TELTLKPGTLTLAQLRAIHAAPVRLQLDASAAPAIDASVACVEQIIAEDRTAYGINTGFGLLASTRIASHDLENLQ KYREPEKYIELDGLTTEDLVNLGKGRYKIKLTPTAEKRVQKSREVIDSIIKEKTVVYGITTGFGKFA-RTVIPINKLQLQ VLAPPTKLLILDGNSPEDLVRCEKGECAIQLSMESEDRIRKARTFLEKIASEHRAVYGVTTGFGTFSNVTIPPEKLKKLQ --MIEIDGRSLRVEDVYAVAVEYDRVSISDDTLKAVEEKHEAFLKLINSGKTVYGVNTGFGSLLNVHIERDQEIELQ KYREPEKYIALDGDSTEDLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIKERTVVYGITTGFGKFA-RTVIPANKLQLQ KYREPEKYIALDGDSTEDLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIKERTVVYGITTGFGKFA-RTVIPANKLQLQ KYREPEKYIALDGDSTEDLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIKERTVVYGITTGFGKFA-RTVIPANKLQLQ --MNALTLTPGTLTLAQLRQVWQQPLQLTLDESAHEAINDSVACVEAIVAEGRTAYGINTGFGLLAQTRIATHDLENLQ --MGEMISLDGPLTWREIASIAEGASLDLSGPARLRIAQARRIVDALVERGIRGYGINTGVGALCDVIISRENQQALS ----LRPGSVPLSDLETIYWTGAPARLDAAFDAGIAKAAARIAEIVAGNAPVYGINTGFGKLASIKIDSSDVATLQ MSDLPSVVFGDGPLRWQELVAVARHGARLELSAAAWARIDNARAIVCRIVANGERAYGISTGLGALCDVLLEGEQLAELS -MSDTRIDAADREALO

Figure 14 /

## Title: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106

JUN 0 3 2003 E

160

RSLIRSHAAGMGE PVEREVVRALMFLRAKTLASGRTGVR PVVLETMVGMLNAGIT PVVREYGSLGCSGDLAPLSHCALVL

81

100.08

65.48 46.88

SWALL: HUTH\_STRGR SWALL: HUTH\_DEIRA

SWALL:CAC21618

983831

66.18

.0

SWALL: BAB1615

**4** S

SWALL: Q9KWE4

. %

42

40.48

SWALL: HUTH BACSU

9 ~

 $\omega$   $\omega$ 

SWALL:Q9KSQ4 SWALL:Q9HU85 SWALL:Q9KBE6

42

FREVVRALMFLRLKTVASGHTGVRPEVAQTMADVLNAGITPVVHEYGSLGCSGDLAPLSHCALTL TEDIVRLIMALKLISLGRGASGVRLELVRLIEAMLDKGVIPLIPEKGSVGASGDLAPLAHMAAVM HNLIVSHAIGMGEPLPAEVVRGMLLLRAQSLSLGHSGVRVEVVELLLALLNADALPVVPSQGSVGASGDLAPLAHLALGL LPENVVRLIMALKLISLGRGASGVRIELIRLIEGMLEKGVIPVIPEKGSVGASGDLAPLAHMSATM RNLILSHCCGVGAPLPENVVRLIMALKLISLGRGASGVRIELIRLIEGMLEKGVIPVIPEKGSVGASGDLAPLAHMSATM ISDETVRLMMLLKINSLARGYSGIRLEVIQALIELVNNQIYPCVPKKGSVGASGDLAPLAHMSTVL RSIVLSHAAGVGEALDDAMVRLVMLLKVNSLARGFSGIRRKVIDALIALINAEVYPHIPLKGSVGASGDLAPLAHMSLVL HNLIYSHACGVGSPFPETVSRTMLVLRANALLKGFSGVRPLVIERLLALVNANIHPVIPQQGSLGASGDLAPLSHLALVL KNLIRSHSSGVGDYLENRYVRAIMAVRLNSLAAGYSAVSADLLNMMVEMLNRDVIPAVPKYGSVGASGDLAPLAHIGLAM SPERCRMLLALRINVLAKGYSGISLETLKQVIEAFNASCLSYVPEKGTVGASGDLAPLSHLALGL RNIVRSHAAGMGPRVEREVVRALMFLRLKTVCSGRTGVRPEVAQTMADVLNAGITPVVHEYGSLGCSGDLAPLSHCALTL LNLILSHACGVGDPFPECVSRAMLLLRANALLKGFSGVRAELIEQLLAFLNKRVHPVIPQQGSLGASGDLAPLSHLALAL RDEQTRAIICAAVANYSQGKSGLDRSLVEGLLALLNHGITPQVPAQGSVGY---LTHMAHVGIAL SPERCRMLLALRINVLAKGYSGISLETLKQVIEMFNASCLPYVPEKGTVGASGDLAPLSHLALGL SPERCRMLLALRINVLAKGYSGISLETLKQVIEAFNASCLSYVPEKGTVGASGDLAPLSHLALGL , DDDIVRLMMVLKINSLARGFSGIRLSVIQALIALVNAGVYSVDPAKGSVGASGDLAPLAHMSLTL RNIILSHACGVGDPLGRVEARAVMAAQIANLTHGYSGVRVETAEMLLALLNADIIPLIPSRGSVGY-----LTHAALVL RSLVLSHAAGIGAPLDDDLVRLIMVLKINSLSRGFSGIRRKVIDALIALVNAEVYPHIPLKGSVGASGDLAPLAHMSLVL apnrarmllalrinilakghsgisvenikkmiaafnafcvsyvpqqgtvgcsgdlcplahlalgi SPERCRMLLALRINVLAKGYSGISLETLKQVIEVFNASCLSYVPEKGTVGASGDLAPLSHLALGL DTAAVRALLVTRLNALAKGYSGIRERVLDVLVGLLNEGVHPVVPSRGSLGASGDLAPLAHMSRVL RNIVRSHAAGMGPRV KSIVLSHAAGIGELM RNLILSHCCGVGQPI VNLVRSHSSGVGKPL RNLILSHCCGVGAPI RNTLLSHACGVGEPI VNLVRSHSSGVGKPI LNLIRSHATGYGEPI VNLVRSHSSGVGKPI ANLVRSHAAGAGSEI VNLVRSHSSGVGKPI RSLVLSHAAGVGEPI

39.28

SWALL: HUTH\_HUMAN

12 13 14

. 8%

38

CAEEL

SWALL: HUTH CA SWALL: Q9HLI6

41.78

39

41.78

SWALL: HUTH PSEPU

10

SWALL: HUTH RHIME

11

SWALL: Q9HU90

. 48

40

41.08

.6%

38

SWALL: HUTH MOUSE

15 16 SWALL:BAB29407 SWALL:HUTH\_RAT SWALL:AAG53586

17

18

19 20

SWALL:Q9KKEO SWALL:Q9HQD5

38

Figure 14, cont.d

### Title: CLONING, OVEREXPRESSION THERAPEUTIC USE OF BIOAC HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS **DOCKET NO.: 078728/0106**

IGEGQA-DVAGERMPAAEALAAADLEPVTLQAKEGLALINGTQLTTGVAALALVDAERVLRSADTAGALTTEVTMSTTAS

SWALL: Q9HQD5



240

PSKDALAKAGLSPVVLAAKEGLALINGTQTSTALALAGLFRAHRAAQSALVTGALSTDAAMGSSAP LGEGQAR-YNGKIISGLEAMKIAGLEPITLAPKEGLALLNGTQASTAFALEGLFVAEDLFASATVCGAMSVEAALGSRRP **PAGELLAAHGIAPVELREKEGLALLNGTDGMLGMLVMALADLDTLYKSADITAALTMEALLGTDRV** PAADVLAELGLS PVQLQAKEGLAL INGTQLMGSLLALALHDAQVLLGTANLAAAMTVEARYGSHR P MGEGEAF-YQGVQMPSKDALAKAGLSPVVLAAKEGLALINGTQTSTALALAGLFRAHRAAQSALVTGALSTDAAMGSSAP IGQGEVF-FEGERMPAMTGLKKAGIQPVTLTSKEGLALINGTQAMTAMGVVAYIEAEKLAYQTERIASLTIEGLQGIIDA IGESRARH-RGEWLPAAEALAVAGLEPLTLAAKEGLALLNGTQVSTAYALRGLFEAEDLFAAATVCGGLSVEAMLGSRAP LGEGKAR-YKGQWLSATEALAVAGLEPLTLAAKEGLALLNGTQASTAYALRGLFYAEDLYAAAIACGGLSVEAVLGSRSP MGHGEAFFAGERMKGDAALKA-AGLSPVTLAAKEGLALINGTQVSTALALAGLFRAHRAGQAALITGALSTDAAMGSSAP LGIGEVS-YRGSVVPAAAALAAEGLATVRLGAKDGLCLVNGTPCMTGLACLALDDAQRLAQWADVIGAMSFEALRGQLAA DAKYVLEAHGLKPVILKPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALTLEVLKGTTKA **LGEGKMWSPTTGWQPADVVLKKNNLEPLELGPKEGLALINGTQMVTALGAYTLERAHNIARQADVIAALSLDVLKGTTRA** DAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEALERASAIARQADIVAALTLEVLKGTTKA IGEGKMWSPKSGWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEALERASAIARQADIVAALTLEVLKGTTKA IGEGKMWSPKSGWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALTLEVLKGTTKA LGEGKAR-YRGEWLPAATALQKAGLAPVTLAAKEGLALLNGTQASTAFALRGLFEAEDLFASAVVCGALTTEAVLGSRRP PV PEL FAEAGLT PVELAEKEGLALVNGT DGMLGQLIMALADL DELLDIADATAAMSVEAQLGT DQV PAGELLAAHGIAPVELREKEGLALLNGTDGMLGMLVMALADLRNLYTSADITAALSLEALLGTDKV KASFALKEEEIEPITLTAKEGLALINGTQAMTAMGVIAYLEAEKLAFQSEIIASLTMEGLRGIIDA DSARALEKAGLKPYQFKEKEGVALINGTSFMSGILSIAVMDAHDILENAIRSALLSFEALGGTSKA MGEGEAF-YQGVQMI LGEGEVF-YKGTKT) VGEGKMWSPKSGWAI IGEGKMWSPKSGWAI MGEGEATDAHGDIR MGEGDAEGPDGTVR MGEGEAEGPDGTVR IGLGDI-EYQGQVR MGEGKAF-FEGRLM

Figure

IGHGSAMQGTERLSGADAL-ARLGLAPLRLEAKEGLSLVNGTPCATGLAALALARTERLFAWADAAAAMTYE-NLGSQAN 161 66.18 65.48 42.0% 40.48 42.28 41.78 41.78 40.68 40.78 39.28 38.88 41.08 38.68 38.68 39.3% 100.0% 46.88 SWALL: HUTH STRGR SWALL: HUTH DEIRA SWALL: HUTH PSEPU SWALL: HUTH RHIME SWALL: HUTH HUMAN SWALL: HUTH BACSU SWALL: HUTH MOUSE CAEEL SWALL: BAB16159 SWALL: CAC21618 SWALL: BAB29407 SWALL: AAG5358 SWALL: Q9KBE6 SWALL: Q9HU90 SWALL: Q9HLI6 SWALL: Q9KWE4 SWALL: Q9KSQ4 SWALL: Q9HU85 SWALL: Q9KKEO SWALL: HUTH SWALL: HUTH 983831 10 12 13 15 16 2 9 4  $\boldsymbol{\omega}$ σ 14

## CORT 142 Figure

320

<u> JGRSAQNMFAFLADSPIVASHREGDGRVQDAYSLRCSPQVTGAARDTIAHARLVATRELAAAIDNP</u>

FRAELHEPLRPHPGC

241

100.0%

99

SWALL:CAC21618

983831

46. 42 42

SWALL: HUTH STRGR SWALL: HUTH DEIRA

SWALL: BAB16159

### AG, OV EUTIC USE OF AIDINE AMMONIA LE INTOR(S): Joseph ROBERTS et DOCKET NO.: 078728/0106 Title: CLONING, OVEREXPRESSION THERAPEUTIC USE OF BIOA HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS

FQPDV-VGLRPHPGALAVAAELREFLAGSEIAPSHLTGDGKVQDAYSLRAVPQVHGATWDALAQAERVLAVEFASVTDNP FHPDIHT-LRGHKGQIDAGSALRNLLQGSEIRESHIEGDERVQDPYCIRCQPQVDGACLDLLASVARTLEIEANAVTDNP FDEQIHFA-RGYVEQVDVARRMESYLQDSQLTT--RQGELRVQDAYSLRCIPQVHGATWQTLRYVKEKLEIEMNAATDNP FDTDIHA-LRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKNIITTELNSATDNP FTPWILGA-RPHLGQVAIGNRFREYLTGSDIV--KRADSVKVQDAYTLRCIPQVYGSVADVIDYVENVLSVEINSATDNP LAPELHA-IRPHPGQGVSADNMSRVLAGSGLTGHHQDDAPRVQDAYSVRCAPQVNGAGRDTLDHAALVAGRELASSVDNP FHPDIHT-LRGHKGQIDAGSALRNLLQGSEIRESHIEGDERVQDPYCIRCQPQVDGACLDLLASVARTLEIEANAVTDNP FDEDIHLA-RGYQEQIDVAERIRFYLSDSGLTTS--QGELRVQDAYSLRCIPQVHGATWQTLGYVKEKLEIEMNAATDNP FDPRIHR-VRGHRTQMDAATAYRHLLVSSEIGQSHSNCE-KVQDPYSLRCQPQVMGACLQQIRSAAEVLEVEANSVSDNP FDARIHAA-RGQRGQIDVAAAYRDLLASSEVARSHEKCD-KVQDPYSLRCQPQVMGACLTQMRQAAEVLEIEANAVSDNP FDARIHEA-RGORGOIDTAACFRDLLGDSSEVSSHKNCD-KVODPYSLRCOPOVMGACLTOLROAAEVLGIEANAVSDNP FHPDIQHCAAIRARSTRAAA-LRQLLTGSPIRQSHIEGDERVQDPYCIRCQPQVDGACLDLLRSVAATLTIEANAVTDNP FDAEI-VALKPHPGMQRVAANLRALLAGSQVLENAR--GIRTQDALSIRSIPQIHGACRDQLAHARQIET-ELNSATDNP YDPDIHR-IRPHRGONLSALRLRALLNPSQIAESHRNCT-KVQDAYTLRCVPQVHGVVHDTIEFVREIITTEMNSATDNP FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSATDNP FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSATDNP FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSATDNP FDARIHE-VRGQRGQIDAAALFRHVLTDTSAIASHHNCD-KVQDPYSLRCQPQVMGACLTQMRQVAEVLLVESNAVSDNP SAVGEGLRDWLADSPMLAG--TAGTRTQDPLSLRAVPQVHGAARDAFGQVAEIVDRELASVTDNP AVSARHIRNLTAGSEVLDHHRDCD-RVQDAYSIRCLPQVHGAVRDALDHLRAAVATELNSATDNP LAPELHA-IRPHPGQAASAANMAAVLKGSGLTGHHQDDAPRVQDAYSVRCAPQVAGAGRDTMAHAGLVAERELAAAVDNP CAPAIHE-VRPHDGQ AFAELPLALRQSPGL 39.38 39.28 38.8% .0% 40.48 . 68 . 68 . 0 .0% . 68 65.4 42.29

41.

SWALL: HUTH\_PSEPU

10

SWALL: Q9KBE6

SWALL: Q9HU85

ထတ

SWALL:HUTH RHIME

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SWALL: Q9HU90

12 13

41

SWALL: HUTH BACSU

SWALL: Q9KWE4

SO

SWALL: Q9KSQ4

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38 38 38

SWALL: HUTH MOUSE

SWALL: BAB29407 SWALL: HUTH RAT

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39

SWALL: AAG53586

19 20

18

SWALL: Q9KKE0 SWALL: Q9HQD5

41

SWALL: HUTH HUMAN SWALL: HUTH CAEEL SWALL: Q9HLI6

14 15 16



# Title: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106

JUN 0 3 2003

PADEIAARK OF

### 400

321

STRGR

SWALL: HUTH

SWALL: CAC21618

983831

Figure

SWALL: HUTH DEIRA

SWALL: BAB1615

SWALL: HUTH BACSU

9

SWALL: Q9KWE4

SWALL: Q9HU85

 $\omega$   $\omega$ 

SWALL: Q9KSQ4

SWALL: Q9KBE6

#### HGAPVAYVLDFLAIAVADLGSIAERRTDRMLDPARSRDLPAFLADDPGVDSGMMIAQYTQAGLVAE HGAPVAYVLDFLAVAVADLGSIAERRTDRLLDKNRSHGLPPFLADDAGVDSGLMIAQYTQAALVGE HAEPVAMAADNLALAIAEIGSLSERRMALLIDSALSK-LPPFLVDNGGVNSGFMIAQVTAAALASE LVFAAGDVISGGNFHAEPVAMAADNLALALAEIGSLSERRISLMMDMHMSQ-LPPFLVANGGVNSGFMIAQVTAAALASD HAEPVAFAADQIALAVCEIGAISQRRIALLVDPALSLRLPAFLAKKPGLNSGLMIAEVTSAALMSE HGEYPAKALDYLAIGVHELAAISERRÍERLCNPSLS-ELPAFLVAEGGLNSGFMIAHCTAAALVSE **VVLPDGRVESNGNFHGAPVAYVLDFLAIVAADLGSICERRTDRLLDKNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSE** LIFPTGEVVSGGNFHGQPLAVTIDALKVAVAELGSISERRTEQLLNPALS-GLPAFLTPNGGLNSGFMIAQYTSAALVSE **HAEPVAFAADQTALAVCEIGAIAQRRIALLVDPALSYGLPAFLSKKPGLNSGLMIAEVTSAALMSE HAEPVAFAADQTALAVCEIGAIAQRRIALLVDPALSYGLPAFLSKKPGLNSGLMIAEVTSAALMSE** HGQQIALAMDFLGIAMAELANISERRIERLVNPQLN-DLPPFLSAAPGVQSGVMILQYCAASLVSE HGEYPAKALDYLAIGVHELAAISERRIERLCNPSLS-ELPAFLVAEGGLNSGFMIAHCTAAALVSE MVFASGETISGGNFHGEYPAKALDYLAIGVHELAAISERRIERLCNPSLS-ELPAFLVAEGGLNSGFMIAHCTAAALVSE HGQPIAFAMDFLKIAISELANIAERRIERLVNPQLN-DLPPFLSPHPGLQSGAMIMQYAAASLVSE LVFAAGDVISGGNFHAEPVAMAADNLALAIAEIGSLSERRISLMMDKHMSQ-LPPFLVENGGVNSGFMIAQVTAAALASE HGEYPAKALDYLAIGIHELAAISERRIERLCNPSLS-ELPAFLVAEGGLNSGFMIAHCTAAALVSE HGEYPAKALDFLAIAVAELAQMSERRLERLVNKELS-GLPTFLTPDGGLNSGFMTVQLCAASLVSE L-FNGEEVVSGGNFHGEPVALAADFLAIALTDLGNMVERRIARLVDTNLS-GLPPFLTPDSGLNSGYMIPQYTAAALCNR HGEVLALRLGYAASALAELAAISERRTDRLLNPETQEPLEPFLAPDSGLHSGLMIPQYTAASLVND HGESVAMAADLLAIAVAELGGVAERRLDRLVNPLVS-GLPAFLVGKPGVNSGMMITQYVAASLAGE HAEPVAMAADNLALAIAEIGALSERRIALMMDKHMSQ-LPPFLVRNGGVNSGFMIAQVTAAALASE VGAALGLAMDSLAVAVAEVAAISERRIDRLVNPLVS-GLPAFLAGDSGVSSGFMIAQYTAAALVAE LLLGTPEVVSQANP MVFANGETVSGGNF AVAGSPEVHSQAHA VVLPSGEVTSNGNF LVLSDNSVVSGGNF LVLSDNSVVSGGNF LIFNDGDVISGGNF LVFADGDIISGGNF LIFDNGQVISGGNE LVLSDNSVVSGGNF VVLPDGRVESNGNF LVFADREIISGGNF MVFASGETISGGNF MVFASGETISGGNF LVFAANEMVFRGNF LVFPSGTVVSGGNF 66.18 48 41.78 40.68 41.08 38.2% .0% .0% 39.28 7 **8**6 38.68 89 œ 0 41. <u>ი</u> 42. 40. 38. 38. 65 46 42 40 39

SWALL: HUTH HUMAN SWALL: HUTH CAEEL

SWALL: Q9HU90

12 13

SWALL:HUTH\_PSEPU SWALL:HUTH\_RHIME

10

SWALL: HUTH MOUSE

SWALL: Q9HLI6

15 16

14

SWALL:BAB29407 SWALL:HUTH RAT

SWALL: AAG5358

SWALL:Q9KKEO SWALL:Q9HQD5

# Figure

401

100.08 66.18

SWALL: CAC21618

983831

480

NKRLAVPASVDSIPSSAMQEDHVSLGWHAARKLRTSVANLRRILAVEMLIAGRALDLRAPLKPGPATGAVLEVLRSKVAG

**LKRLAVPASADSIPSSAMQEDHVSMGWSAARKLRTAVDNLARVIAVELYAATRAIQLREGLTPAPASQAVVEAVRAAVEG** 

### le: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106

*			
٠,	LRSLGQP-TLDNASVSGAQEDHVSMSAGAAYNFREAVEKAATVVGVELLCGAQGREFLDPLALGAGTAAAYDLVR-EVSE	42.28	SWALL: Q9HQD5
	NRRLAAPASLDGGITSALQEDMLTHATPAAWKALSIVDNLERILAIELLAAHRPMSCSRKRRARRNAPLPFTGTYARRSP	38.98	SWALL: Q9KKE0
	NKGLCHPTSVDK-PPSANQEDHVSMAPAAGRRLWEMAGNTRGVLAVEWLAACQGADLRDGLTSSPLLEQARQSCGEQVAH	39.8%	SWALL: AAG53586
	SKALCHPSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRPLKTTTPLEKVYDLVRSVVRP	38.28	SWALL: HUTH RAT
	SKALCHPSSVDSLSTSAATEDHVSMGGWAARKALRVVEHVEQVLAIELLAACQGIEFLRPLKTTTPLEKVYDLVRSVVRP	38.68	SWALL: BAB29407
	SKALCHPSSVDSLSTSAATEDHVSMGGWAARKALRVVEHVEQVLAIELLAACQGIEFLRPLKTTTPLEKVYDLVRSVVRP	38.68	SWALL: HUTH MOUSE
	NKVLAYPSSADTIPTSANQEDHVSMGATGSLKLLEIIDNVRYIIAIEYLLGSQALEFTDK-GMSPSTRKIYEKIREKVEK	41.08	SWALL:Q9HLI6
	NKVLCHPSSVDSIPTSCNQEDHVSMGGFAARKALTVVEHVEAVLAMELLAACQGIEFLKPLISTAPLHKIYQLVRS-VAP	38.88	SWALL: HUTH CAEEL
	NKALCHPSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRPLKTTTPLEKVYDLVRSVVRP	39.28	SWALL: HUTH HUMAN
	NRQLAQPAVVDNFVTSALQEDHLSLGTSAALKLGRALENLRRILAIEYLLAAQAFEFLAPQRFGQGTAAAWGILRERVPA	40.78	SWALL: Q9HU90
	NKQLSHPASVDSTPTSANQEDHVSMACHGARRLLQMTENLFSIIGIEALAAVQGIEFRAPLTTSPELQKAAAAVRGVSSS	40.68	SWALL: HUTH RHIME
	NKALSHPHSVDSLPTSANQEDHVSMAPAAGKRLWEMAENTRGVLAIEWLGACQGLDLRKGLKTSAKLEKARQALRSEVAH	41.78	SWALL: HUTH PSEPU
	NKTLAHPASVDSIPSSANQEDHVSMGTIGSRHAYQIIQNVRNVLAIELICAMQAVDIRGREKMASFTKKILEKGREHVPY	39.38	SWALL: Q9KBE6
	NKALAHPASVDSLPTSANQEDHVSMAPNAGKRLWAMAENVRGILAVEWLGACQGLDFREGLKSSPKLEQARRLLRDKVPY	41.78	SWALL: Q9HU85
	NKTLAHPASVDSLPTSANQEDHVSMATFAARRLRDMGENTRGILAVEYLAAAQGLDFRAPLKSSPRIEEARQILREKVPF	42.28	SWALL: Q9KSQ4
	NKTLAHPASVDSIPSSANQEDHVSMGTIAARHAYQVIANTRRVIAIEAICALQAVEYRGIEHAASYTKQLFQEMRKVVPS	40.48	SWALL: HUTH BACSU
	NKQMSHPASVDSTPTSANQEDHVSMACHGARRLLAMTDNLFGILGIEALAAVQGVELRGPLKTSPELEKAAAVLRSAVPV	42.08	SWALL:Q9KWE4
	NKQMSHPASVDSTPTSANQEDHVSMACHGARRLLAMTDNLFGILGIEALAAVQGVELRGPLKTSPELEKAAAVLRSAVPV	42.08	SWALL: BAB16159
	NKVLSHPASVDSIPTSANQEDHVSMGAHAARQLRQIVANVQTVLSIELLCAAQGLDFQQ-LRAGRGVQAAYEYVRTFVPT	46.88	SWALL: HUTH DEIRA
	MKRLAVPASADSI PSSAMQEDHVSMGWSAARKLRTAVDNLARIVAVELYAATRAIELRAALTPAPASEAVVAALRAAGAG	65.48	SWALL: HUTH STRGR

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### Title: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOACE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106



		481	_ ·
983831	831	100.0%	<b>PGQDRFLSAELEAAYDLLANGSVHKALEAHLPA</b>
SWA]	SWALL: CAC21618	66.18	PGPDRHLAPDLAAADAFVRAGHLVAAAESVTGP
SWA]	SWALL: HUTH STRGR	65.48	<b>PGPDRFLAPDLAAADTFVREGRLVAAVEPVTGP</b>
SWA]	SWALL: HUTH_DEIRA	46.8%	LTEDRYFRPDLLRLRGELVSGRVAQAADTQAPA
SWA]	SWALL:BAB16159	42.08	LEDDRYMATDLKAAIEVVASGALVSAISSGLPV
SWA1	SWALL:Q9KWE4	42.0%	LEDDRYMATDLKAAIEVVASGALVSAISSGLPV
SWA1	SWALL: HUTH BACSU	40.48	IQQDRVFSYDIERLTDWLKKESLIPDHQNKELR
SWA1	SWALL: Q9KSQ4	42.28	YDKDRYFAPDIEKANALL-QLAVHNRLMPDQLL
SWA1	SWALL:Q9HU85	41.78	YQEDRFFAPDIEAASQLLASGCLNALLPARLLP
SWA1	SWALL:Q9KBE6	39.3%	IDQDRMFAKDIERAAKWLKDGSWDFTKMREKER
SWA1	SWALL: HUTH_PSEPU	41.78	YDRDRFFAPDIEKAVELLAKGSLTGLLPAGLPS
SWAI	SWALL: HUTH_RHIME	40.68	<b>IEEDRYMADDLKAAGDLVASGRLAAAVSAGLPK</b>
SWAI	SWALL:Q9HU90	40.78	YDTDRWLAPDIASAAAILGERKSLARLAASIGD
SWAI	SWALL: HUTH_HUMAN	39.28	WIKDRFMAPDIEAAHRLLLEQKVWEVAAPYIEK
SWAI	SWALL: HUTH CAEEL	38.8%	<b>PNEDRYMKPEIDAVLEMIRENRIWEAVLPHLET</b>
SWAI	SWALL: Q9HLI6	41.0%	LDHDRPPSFDIETIRKMMDKKEFISALP
SWAI	SWALL: HUTH MOUSE	38.68	WIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEK
SWAI	SWALL:BAB29407	38.68	WIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEK
SWAI	SWALL: HUTH_RAT	38.2%	WIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEK
SWAI	SWALL: AAG53586	39.8%	YDDDRFFAPDIEAAISLLNKGSLVGLLPAFL
SWAI	SWALL: Q9KKE0	38.9%	PIATIVR
SWAI	SWALL:Q9HQD5	42.28	PAGDRALADDMAAVGDLVRAGLVEDAVARALDA

14 E

Figure

### Title: CLONING, OVEREXPRESSION AND THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106



# Figure

HAL 983831

KEY:

coelico Streptomyces CAC21618

griseus Streptomyces STRGR

Deinococcus radiodur DEIRA HUTH

Agrobacterium rhizog BAB16159

Agrobacterium rhizog Q9KWE4

Bacillus subtilis HUTH BACSU

S aerugino cholerae Pseudomonas Vibrio **29ни85** Q9KSQ4

α

Bacillus halodurans Q9KBE6

Pseudomonas putida Rhizobium meliloti PSEPU HUTH HUTH

aerugino Pseudomonas Human RHIME HUTH HUMAN Q9HU90

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S

Caenorhabditis Thermoplasma CAEEL HUTH\_C? Q9HLI6 11 12 13 14 15 16

elegan

acidoph

(Mouse) Mus musculus Mouse MOUSE HUTH\_

BAB29407

pCosAS1 uncultured bacterium RAT AAG53586

Rhizobium meliloti

Halobacterium

# Title: CLONING, OVEREXPRESSION AN THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106



\*\*\*\*\*\*

Figure

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VVVGTSGTTAEDVVAVARHGARVELSAAAVEALAAARLIVDALAAKPEPVYGVSTGFGAL ITLGLSGATADDVIAVARHEARISISPQVLEELASVRAHIDALASADTPVYGISTGFGAL * ** ** ** ** ** ** ** ** ** ** ** ** *	ASRHIGTELRAQLQRNIVRSHAAGMGPRVEREVVRALMFLRLKTVASGHTGVRPEVAQTM ATRHIAPEDRAKLQRSLIRSHAAGMGEPVEREVVRALMFLRAKTLASGRTGVRPVVLETM * ***	ADVLNAGITPVVHEYGSLGCSGDLAPLSHCALTLMGEGEAEGPDGTVRPAGELLAAHGIA VGMLNAGITPVVREYGSLGCSGDLAPLSHCALVLMGEGEATDAHGDIRPVPELFAEAGLT ************************************	PVELREKEGLALLNGTDGMLGMLVMALADLRNLYTSADITAALSLEALLGTDKVLAPELH PVELAEKEGLALVNGTDGMLGQLIMALADLDELLDIADATAAMSVEAQLGTDQVFRAELH **** ******* ****** * ****** * ********	A-IRPHPGQGVSADNMSRVLAGSGLTGHHQDDAPRVQDAYSVRCAPQVNGAGRDTLDHAA.  EPLRPHPGQGRSAQNMFAFLADSPIVASHREGDGRVQDAYSLRCSPQVTGAARDTIAHAR.  ****** ** ** ** ** ** ** ** ** ** ******	LVAGRELASSVDNPVVLPDGRVESNGNFHGAPVAYVLDFLAIVAADLGSICERRTDRLLD LVATRELAAAIDNPVVLPSGEVTSNGNFHGAPVAYVLDFLAIAVADLGSIAERRTDRMLD
9 /	99	126 127	186	246 247	305
STRG "HAL"	STRG, HAL	STRG	STRG HAL	STRG HAL	STRG HAL

### Title: CLONING, OVEREXPRESSION AN THERAPEUTIC USE OF BIOACTIVE HISTIDINE AMMONIA LYASE Inventor(s): Joseph ROBERTS et al. DOCKET NO.: 078728/0106

SMG	( + 5
IRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEMKRLAVPASADSIPSSAMQEDHVSMG	O TOTAL TO THE CONTRACT OF THE STATE OF THE
SSAMO	
ADSIP	T 1 2 C 1
<b>VPAS</b>	10 K CT 7
IKKLA	K T 1771
LVSEN	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
TOAA	( K ( E)
MIAQY	V C K T V K
DSGL	
DDAGV	
PFLA	K + C + C
SHGLE	7 7 7 7
KNRS	ر د
365	770

Figure 15, Cont.d.

WURRINGEN DINEARY FAVENT, TAGRALDI, RAPIKPGPATGAVI, EVI, RSKVA-GPGO	10	HAT.
WSAARKLRTAVDNLARIVAVELYAATRAIELRAAEGLTPAPASEAVVAALRAAGAEGPGP	425	STRG
* ********** ****** * * * * * * * * * *		
PARSRDLPAFLADDPGVDSGMMIAQYTQAGLVAENKRLAVPASVDSIPSSAMQEDHVSLG	367	HAL
KNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEMKRLAVPASADSIPSSAMQEDHVSMG	365	STRG

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DRFLSAELEAAYDLLANGSVHKALE

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DRFLAPDLAAADTFVREGRLVAAVE

485

STRG